Corticosteroid-Induced Bone Loss Occurs Within 3 Months

BY PATRICE WENDLING

CHICAGO — Fracture risk increases in arthritis patients within about 3 months of starting corticosteroids and remains high, according to Dr. Nelson Watts.

“How much of this is steroids and how much of this is the underlying disease is unanswered,” said Dr. Watts, an endocrinologist and director of the bone health and osteoporosis center at the University of Cincinnati.

Glucocorticoid-induced osteoporosis results from a variety of systemic effects of corticosteroids, but it’s the combination of reduced bone formation and increased bone resorption that causes a “double whammy” for patients—a troubling aspect for rheumatologists, who regularly dispense corticosteroids for their patients, Dr. Watts said at a symposium sponsored by the American College of Rheumatology.

The exact dose at which corticosteroids increase fracture risk is also difficult to tease out because of the underlying disease. One study observed that fracture risk was dose dependent and significantly higher with 2.5 mg/day or more of oral prednisone, with increases of 61% in hip and 160% in vertebral fractures (J. Bone Miner. Res. 2000;15:993-1000).

“It may well be that people who need 2.5 mg/day of prednisone are at increased fracture risk because of prednisone, but because of their rheumatoid arthritis; … clearly, as the dose goes up, the risk increases,” he said.

The American College of Rheumatology’s current guidelines on glucocorticoid-induced osteoporosis highlight lifestyle modifications, such as calcium and vitamin D supplementation, weight-bearing exercise, and minimization of alcohol intake.

The value of calcium and vitamin D supplementation is unclear, Dr. Watts said. In a relatively small trial in 96 RA patients on prednisone, daily supplementation with 500 IU of vitamin D and 1,000 mg of calcium carbonate per day significantly improved bone mineral density, at a rate of 0.72% in the lumbar spine and 0.85% in the trochanter per year, compared with losses of 2% and 0.9%, respectively, among patients not taking the supplement (Ann. Intern. Med. 1996;125:961-8).

In four prospective studies in 173 patients who recently started corticosteroid therapy, however, bone loss occurred at a rate of 3%-5% per year, despite daily supplementation with the equivalent of 1,000 mg of calcium. Two other studies that Dr. Watts highlighted reported no bone loss in patients who were given up to 1,000 mg per day of calcium and up to 500 IU per day of vitamin D.

Pooled data showed a significant 70% decrease in vertebral fractures with rise-dronate vs. placebo, Dr. Watts said. New prescribing information also shows that bone mineral density changes were significantly better with zoledronic acid than alendronate.

Dr. Watts disclosed relationships with Amgen Inc., Eli Lilly & Co., Procter & Gamble Co., Sanofi-Aventis, Novo Nordisk Inc., and Novartis Pharmaceuticals Corp., which manufactures Reclast.

Golimumab Approved for RA, PsA, Ankylosing Spondylitis

BY ELIZABETH MECHTIE

Golimumab, the first once-monthly, injectable tumor necrosis factor–alpha antagonist, was recently approved for treating adult patients with moderately to severely active rheumatoid arthritis, active psoriatic arthritis, and active ankylosing spondylitis, based on data from five studies of more than 2,500 patients.

The Food and Drug Administration approved the TNF inhibitor for use in combination with methotrexate in patients with RA; with or without methotrexate for psoriatic arthritis; and for use alone in patients with ankylosing spondylitis. It was not approved for pediatric use. Recommended dosage (50 mg administered subcutaneously once a month) is the same for all indications.

Golimumab will be marketed as Simponi by Centocor Ortho Biotech Inc., and has been available since its approval on April 24, according to a spokesperson for the company. The annual cost of golimumab is $18,900, which is based on the list price and is comparable with the cost of other concomitant biologics that are used to treat these three indications, he said.

Medicare and some private insurance carriers have adopted a fourth tier of copayment that requires patients to pay 40% of the price of particularly costly drugs.

Dr. John Kay, a lead investigator in the phase II and III trials, said in an interview that “having another TNF antagonist available allows patients who are inadequate responders to one or more of the currently available TNF agents to have an alternative agent to treat their disease.”

Golimumab “can be dosed less frequently, allowing the patient more flexibility,” said Dr. Kay, director of clinical trials in the rheumatology unit at Massachusetts General Hospital, Boston.

Dr. Kay served as a consultant to Centocor and as a member of the steering committee for clinical trials; he was on the steering committee for the GO-AFTER (Golimumab After Former Anti-TNF Therapy Evaluated in RA) study of 461 patients who were treated previously with at least one anti-TNF-alpha treatment and had stopped treatment for various reasons.

Approval for the three indications was based on five simultaneous phase III trials of more than 2,000 patients with RA, psoriatic arthritis, and ankylosing spondylitis, which included three studies of 1,542 patients with moderately to severely active RA who had had the disease for 1-9 years.

The three RA studies were the GO-AFTER study and two other studies (one that evaluated golimumab in 637 patients who were naive to methotrexate and who had not been previously treated with a TNF-blocker, and another that evaluated golimumab in 444 patients with inadequate responses to methotrexate). In the three studies, a greater proportion of patients achieved American College of Rheumatology responses at 12 weeks (in two studies) and 24 weeks (all three studies), compared with the proportion of patients achieving those responses on methotrexate alone.

As with other TNF blockers, the label for golimumab has a boxed warning about the risk of tuberculosis and invasive fungal infections associated with treatment, and the FDA is requiring a risk evaluation mitigation strategy to address the potential serious risks associated with golimumab.